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ABSTRACT

Dialysis encephalopathy is a progressive neurological disorder occurring after long-term hemodialysis in some renal failure patients. Accumulation of aluminum in the brain is suspected as its cause, and the use of reverse osmosis of the dialysis water and administration of desferrioxamine to the patient have been successful in reducing the accumulation of aluminum. Typical communication disorders in patients with dialysis encephalopathy include forms of dysfluency, articulatory dysfunction, disorders of phonation and prosody, language deficits, and generalized neuropsychological disturbances, including dementia. A case study of one 48-year-old female patient found that the use of reverse osmosis and desferrioxamine stopped the progression of the disease and brought about a perceptible improvement of functions. It is also concluded that early and careful assessment of speech and language functions is important for the early detection and treatment of dialysis encephalopathy. (MSE)

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SPEECH AND LANGUAGE DISORDERS IN A DIALYSIS ENCEPHALOPATHY PATIENT AND THE EFFECT OF DESFERRIOXAMINE AND REVERSE-OSMOSIS WATER TREATMENT

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1. INTRODUCTION

Dialysis encephalopathy (earlier also called "dialysis dementia") is a progressive neurological disorder that occurs after long-term hemodialysis in some patients with chronic renal failure. It was first described by Alfrey & al. (1972) and is the leading cause of death in some renal centres. However, its geographical distribution is very varied, so that in some centres the disease has never occurred (Parkinson & al. 1979). It is characterized by a unique speech disorder, seizures, EEG changes, myoclonus, dysaxiaxia and dementia (Lederman & Henry 1978). Speech and language disorders are often mentioned as the first signs of dialysis encephalopathy (Madison & al. 1977, Barron & al. 1980).

There has been much speculation about the etiology of dialysis encephalopathy, and several causative factors have been suggested, e.g. amino-acid depletion, vitamin deficiency, slow virus infection, abnormal cerebrospinal fluid dynamics, phosphate depletion, a primary seizure disorder, disturbed dopamine metabolism, and disturbances in brain amine neurotransmitter metabolism (O'Hare & al. 1983). Recently, Sweeney & al. (1985) have suggested that a deficiency of a neurotransmitter called GABA might be the immediate cause for dialysis encephalopathy. At present, however, the most widely accepted cause is thought to be the accumulation of aluminium in the cerebral cortex (Davison & al. 1982; O'Hare & al. 1983; Wills & Savory 1983).

The disease was first described in 1972, but no special treatment was invented during the early 1970's; among the treatment methods suggested at that time were e.g. increased dialysis, renal transplantation and various medicines, especially diazepam. But these appeared to have only a temporary effect (Lederman & Henry

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1978). In fact, we have seen two patients who developed the symptoms of dialysis encephalopathy shortly after a successful renal transplantation (Lehtihalmes 1984). The mean duration of clinical course until death has been about six months (Chui & Damasio 1980).

As the accumulation of aluminium in the brain became to be suspected as the cause for dialysis encephalopathy, new methods of treatment were suggested at the turn of the 1980's in order to lower the aluminium concentration in the nervous tissue. Since most of the aluminium accumulated in the brain originates from the water used in hemodialysis and penetrates the blood-brain barrier (Banks & Kastin 1983; Schreeder & al. 1983), it has become necessary to lower the aluminium concentration of the dialysis water with different methods, the most efficient of which has proved to be reverse osmosis (Bok & Grondin 1980; Davison & al. 1982). Deionizing the dialysis water has also been effective (Barron & al. 1980). An additional source of aluminium may be the phosphate binding gels (aluminium hydroxide) taken orally by hemodialysis patients in order to prevent hyperphosphatemia which arises in chronic renal failure. This is why excessive dosages of phosphate binding gels should be avoided, especially with children (Alfrey 1985). Recently it has been shown that desferrioxamine has a good therapeutic effect in dialysis encephalopathy (Milne & al. 1983). It seems to mobilize the aluminium from the tissue to the serum, thus easing removal by hemodialysis (Wills & Savory 1983).

2. COMMUNICATION DISORDERS IN DIALYSIS ENCEPHALOPATHY

In the literature four studies can be found on speech and language disorders in dialysis encephalopathy (Rosenbek & al. 1975; Madison & al, 1977; Baratz & Herzog 1980; Barron & al. 1980). Except for the one by Barron & al. these are case studies and do not contain a systematic analysis of the development of speech and language disorders during the progression of the disease. In these studies the following characteristics have been described as typical of dialysis encephalopathy.

Dysfluency has been consistently mentioned as the most striking feature at the early stages of the disease. Various stuttering-like phenomena have been observed: repetitions of sounds, syllables, words, and sometimes phrases, hesitations, difficulties in initiating phonation and articulation, perseveration of stressed syllables and words, inappropriate pauses within and between words, and even

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intermittent mutism. In general, the speech rate tends to be very slow, and the speech has a very laboured quality. Rosenbek & al. (1975) also report significant abnormalities in diadochokinesis in their patient. Certain disturbances in prosody could also be interpreted as signs of dysfluency: the patients often use an equal stress on every syllable, and their speech has a staccato-like rhythm ("scanning speech"). The "stuttering" is more marked at the early stages of the disease than terminally. The severity of the dysfluency has been shown to fluctuate increasingly towards the terminal stage of the disease, when it alternates between total mutism and hyperfluency (Madison & al. 1977). The classification of this symptom as stuttering has been criticized, and e.g. Rosenbek & al. (1975) and Barron & al. (1980) prefer calling it either dysarthria or dyspraxia (or a mixture of both).

Another disorder that is often mentioned is irregular articulatory dysfunction, which includes imprecise consonants, sound substitutions and omissions with frequent attempts at self-correction. The articulatory movements are irregularly and unpredictably deviant, and the errors tend to increase as sentences become longer. The nonverbal oral-motor functions are also inaccurate and uncoordinated. The articulation errors tend to be phonetic rather than phonemic.

Thirdly, disorders of phonation and prosody have occurred. The type of these disorders, however, seems to be individual to a great extent. The phonation quality has been described as varying from a strain-strangle dysphonia in some patients to breathy phonation in others. The pitch is often monotonous and lower than normal with occasional pitch breaks, especially in conversational speech. In some patients, on the other hand, uncontrollable rising and falling glides in pitch can be heard.

In addition to the above mentioned disorders of speech, various language deficits are sometimes observed. Auditory comprehension has been described as normal or mildly disturbed. The difficulties become more apparent as grammatical and semantic complexity increases. Some mild word-finding problems and paraphasias may be observed at the early stages, but clearer indications of aphasia appear towards the terminal stage. In addition, there are also aphasic disorders in writing and reading.

More generalized neuropsychological disturbances in dialysis encephalopathy have also been mentioned. These include deterioration in memory function, reduced attention span, apraxia, and diminished interest in vocational, family and social activities. Even clear signs of mania have been observed (Jack & al. 1983). With the progression of the disease these symptoms become more severe, and at the final

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stages patients develop generalized dementia with disturbed thought processes, mental confusion, delusions, hallusinations and disorientation.

3. THE PRESENT CASE

The patient is a 48-year-old female factory worker who developed uremia after chronic nephritis in the year 1978. Hemodialysis was begun the following year, three times a week. In summer 1981 she had some mild paroxysmal speech difficulties after dialysis. In summer 1982 after dialysis she had a sudden period of mutism which improved after half an hour. She had also some pains in her ribs and mild mental slowness was observed the following autumn, and the diagnosis of dialysis encephalopathy was made. The aluminium concentration of the tap water in Helsinki is very high and therefore the purification of the dialysis water with reverse osmosis was started. Desferrioxamine (Desferal®, Ciba-Geigy Co. Switzerland) treatment was also started in autumn 1982; the desferrioxamine, 2 g in 100 ml normal saline, has been infused to the venous line of the dialyzer during the last hour of the hemodialysis session once a week.

Brain CT scan was normal in autumn 1982 except for mild atrophy. In spring 1984 an NMR investigation was made and it showed some abnormalities adjacent to the left occipital horn. These changes were taken to be related to encephalopathy. The EEG recordings were taken every six months and some progressive abnormalities were observed (slow wave activity, especially in the left temporal area) at the successive recordings.

During the period of this study a speech pathologist assessed the patient five times, always the day following dialysis. The methods used were the Frenchay Dysarthria Assessment (Enderby 1983; see Fig. 1), the Token Test (De Renzi 1977), a test for word fluency (words per minute) and an assessment of reading and writing abilities. In addition, a neuropsyhological investigation was performed by a psychologist.

The equipment used in the instrumental analysis consisted of a Kay Elemetrics Sona-Graph 6061B and a microprocessor-based digital Speech Processing System (SPS-02).

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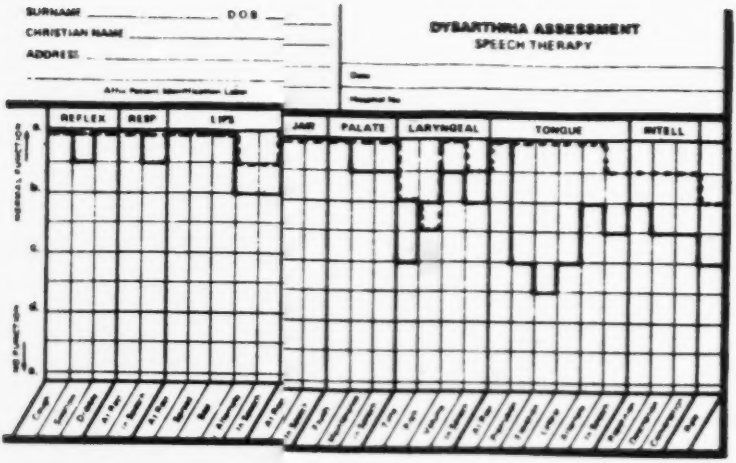

Figure 1. Frenchay Dysarthria Assessment (Enderby 1983) profile of the case at the second (——) and fifth (-----) assessment. Levels a b c d e represent increasing deficiency and have been transformed into numeric scale 0-8 (see table 1).

4. SPEECH AND LANGUAGE FINDINGS

Table 1 shows scores of the Frenchay Dysarthria Assessment (FDA; max = 232), speech rate measured with the reading time (sec) of a short text passage and the average duration of 12 repeated utterances (sec) from the FDA, scores of the Token Test, speech fluency (amount of animals named in one minute), and the aluminium concentration in serum (s-Al; measured during the same month as the speech assessment).

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Table 1. Speech assessment results and serum aluminium concentration during the study (see text).

		Speech rate		Token		s-Al
	FDA	Read.	Repet.	Test	Fluency	(µg/g)
82-10-05	23	39	2.18	35/36	15	0.51
84-04-03	47	55	3.05	34.5/36	16	0.22
84-10-16	27	46	2.24	36/36	--	0.52
85-02-05	20	34	1.98	36/36	20	0.25
85-08-13	14	30	2.02	35.5/36	23	0.24

The results of the Frenchay Dysarthria Assessment indicated a mixture of mild spastic dysarthria and oral apraxia (Fig. 1). The pathological findings were mainly concentrated on tongue movements and laryngeal functions and were most prominent at the second assessment, after which a continuous improvement of functions can be seen. The same trend is evident in speech rate. The intelligibility of speech was rather good all the time. Aphasic symptoms were practically nonexistent; the patient had no naming difficulties, and the Token Test scores were always within normal limits. The patient's reading ability was good and she had no problems in reading comprehension. She had mild dysgraphia which, however, was most likely related to congenital dysgraphia. Speech fluency showed continuous improvement (not measured at the third assessment, unfortunately). An interesting point is that the serum aluminium concentration did not follow the clinical improvement.

No specific neuropsychological disorders could be observed in the assessment by the psychologist and no signs of dementia were apparent. In the following, the most notable disorders in the patient's speech are presented.

4.1. Dysfluency

At the initial stage some sporadic periods of stuttering-like dysfluency and even mutism had been observed after dialysis. The neurologist who first examined the patient reported stuttering, but after that no such features were noticed. However, word- and even syllable-initial sounds were sometimes prolonged, resembling mild forms of stuttering-blocks (Fig. 2). The patient's speech rate was slightly slow, but it

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has been improving after the second assessment (Table 1). The dysfluency may have caused the incorrect realization of the phonological quantity oppositions of Finnish vowels and consonants. Long and short quantity degrees of Finnish were not always adequately differentiated.

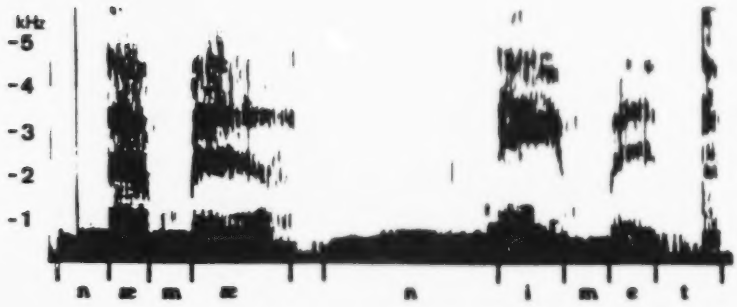

Figure 2. Spectrogram of the words nämä nimet (of the sentence 'näimme vain nämä nimet') repeated by the patient at the third assessment. Note the prolongation of the word-initial [n] of the word nimet.

4.2. Articulation

In general, the patient's speech had a very laboured quality, and some spasticity and difficulties in motor programming of the articulatory movements were obvious. In contrast to the previously described cases, the present patient had almost no trouble with consonant articulation as such. In addition to some sporadic intrusive consonants, such as usva -> usvas (in 'usva nousee suolta') and tutulta -> tuntulta (in 'taulu tuntuu tutulta'), which can be explained as perseveration of syllable structure, the only consonantal error was the tendency of the voiced stops /b/ and /d/, which are not firmly established in the Finnish phoneme system (Karlsson 1982: 57-59), to be irregularly replaced by the corresponding voiceless stops /p/ and /t/. Most of the

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difficulties the patient encountered in consonant articulation seemed to be related to sequential organization of complex articulatory movements. In contrast, the phonetic quality of her vowels was often distorted. The distortion did not appear as consistent phoneme substitutions but rather as irregular inability to reach proper vocal tract configurations for vowels, especially for the short cardinal vowels /i/, /a/, and /u/, which showed some tendency to become centralized, so that /i/ and /a/were realized as [e] (or [ɛ]) and /u/ as [ʉ] (or even [y]). The deviating vowel quality may have been an indication of disturbances in coarticulation. A prominent feature in the patient's speech was the inability to execute sequenced articulatory movements correctly and with proper timing. This could be heard, for example, as "wrong" or "unnatural" labial position in consonant articulation in certain contexts, e.g. the labialisation continuing well over the middle /k/ in the word kaukana. These disturbances were most evident at the first two assesaments and were later practically nonexistent.

4.3. Voice Quality and Prosody

The patient's voice showed some variablity from one assessment to the next. At the first session it was only slightly hoarse. At the second assessment it was worst, with harshness and mild strain-strangle dysphonia. At the next two assesaments the voice quality showed clear improvement and was almost normal at the last session. The pitch was slightly monotonous and somewhat lower than normal at all assessments except the last one, when the pitch range was larger. Word stress was not normally distributed (especially at the second and third assesament), phonologically stressed and unstressed syllables tended to receive almost equal stress, perhaps because of the very slow speech rate. This "scanning speech" character disappeared after the third assesament.

5. DISCUSSION

Dialysis encephalopathy is normally - without any treatment - a fatal disease leading to death in about six months from the beginning of the symptoms. The new methods mentioned above - reverse osmosis, which is used to purify the dialysis water of aluminium, and desferrioxamine, which transfers aluminium from tissues to the blood serum, thus making its removal from the body possible by dialysis -

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obviously stopped the progression of dialysis encephalopathy in our patient, and even brought about perceptible improvement of functions. No dementia developed and the patient's speech dysfluency never reached the stage of stuttering-like features that are so characteristic of other patients previously described in the literature.

Most of the speech disorders of the present case could be described as "timing problems" in the planning and execution of motor schemata. These timing problems could be observed e.g. as prolongation of word- and syllable-initial sounds, which in its turn contributed to the stuttering-like dysfluency. This impaired temporal coordination of articulatory movements was also seen as deviant coarticulatory patterns and as the incorrect realization of the phonological quantity oppositions of Finnish. The patient's speech rate was slow, perhaps partly in order to compensate the difficulties in executing rapid articulatory movements. This slowing down may have caused the abnormal stress patterns by making it impossible to maintain normal coherent stress-groups.

Besides the timing problems the most notable features of the patient's speech disturbances were the distortion of vocal tract configuration in vowel production - a feature not mentioned in earlier reports - and the hoarseness of voice. Nonverbal motor performance was poor in tongue movements and laryngeal functions.

In general, the patient's speech can be characterized as a mixture of dysarthria and dyspraxia. And we believe that this is, in fact, the case with the patients previously described in the literature, too.

A fluctuating course is typical of dialysis encephalopathy; the condition and performance level of the patient may vary within wide ranges from practically normal to almost total inability to communicate. The fluctuation was not marked in the present case, except for some periods of flu, when the patient's performance was somewhat deteriorated. So we believe that the changes in her performance are not due to periodic random fluctuation of the symptoms, but reflect the improving effect of the reverse osmosis water treatment and desferrioxamine on her brain functions.

5.1. Neural Basis of Communication Disorders in Dialysis Encephalopathy

The communicative disturbances in dialysis encephalopathy include both dysarthria and dyspraxia and progress later to more global cognitive and language deterioration, which suggests that cerebral damage is multifocal and diffuse rather than focal (Madison & al. 1977; Barron & al. 1980). In this respect there is a certain

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similarity to acquired dysfluencies/stuttering. Although the neuroanatomic correlates of acquired stuttering are not thoroughly understood at present, most studies have, however, indicated the presence of diffuse or multifocal bilateral lesions in persistent dysfluencies, but some cases of unilateral dominant hemisphere lesions have also been described, most of them transient (Helm & al. 1978; Mazzucchi & al. 1981).

In spite of the symptoms, sometimes very severe, abnormal findings in the nervous tissue have been surprisingly few in dialysis encephalopathy. No anatomical changes have been found at necropsy (Alfrey & al. 1972; Madison & al. 1977; Lederman & Henry 1978; Chui & Damasio 1980). The slight cerebral atrophy and lacunar infarcts in the basal ganglia and thalamus observed by Chokroverty & al. 1976, Baratz and Herzog 1980, and Milne & al. 1983 are not considered to be responsible for the dialysis encephalopathy (Chokroverty & al. 1976). Similarly, the mild CT and NMR abnormalities seen in our case can hardly explain the patient's communication disorders.

The main finding in all previous cases has been the increased content of aluminium in the brain tissue. The concentration of aluminium in the cerebral cortex has been observed to be even 20 times higher than normal control values (Baratz & Herzog 1980). The amount of aluminium in blood serum does not seem to have a positive correlation with the severity of the disorders (Table 1). However, it has been suggested that high aluminium concentration in serum might in fact indicate that the aluminium has been transferred from the nervous tissue to the blood serum (Wills & Savory 1983), thus diminishing the neurotoxic effects of aluminium. This might be the basis of the recovery seen in our patient.

Certain types of EEG changes have proved to be typical of dialysis encephalopathy, i.e. slow-wave activity with bursts of delta waves and high-amplitude spikes (Rosenbek & al. 1975; Madison & al. 1977; Baratz & Herzog 1980). Similar findings were observed also in our patient, the slow-wave activity being most prominent in the left temporal area. The EEG abnormalities have slightly progressed in spite of the clinical improvement of the patient. These changes have been quite mild and they might be due to lowering of vigilance during the recordings, which were made after other examinations on the same day.

The pathogenesis of this disease is not completely understood as yet. The clinical pattern of dialysis encephalopathy is said to reflect more than one etiology, and some other agents may cause similar syndromes (Schreeder & al. 1983). In fact, some sporadic cases of symptoms similar to dialysis encephalopathy have occurred

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even in non-dialyzed patients with renal failure (Wills & Savory 1983). This may be caused by the ingestion of phosphate-binding aluminium gels in order to prevent hyperphosphatemia which arises in chronic renal failure (Alfrey 1985). On the other hand, the syndrome does not appear in all patients exposed to high aluminium, and brain aluminium levels may also be high in dialysis patients without encephalopathy (Sweeney & al. 1985). According to Van de Vyver and De Broe (1985) the relationship between the aluminium concentration in a tissue and its toxic effect is not clear at present. Sweeney & al. (1985) have recently suggested that GABA deficiency in frontal, occipital, and cerebellar cortex, as well as in the caudate nucleus and medial dorsal nucleus of the thalamus might explain some features of dialysis encephalopathy. According to them the communicative disorders in dialysis encephalopathy could be due to GABA deficiency in the thalamus.

6. CONCLUSION

Barron & al. (1980) studied 60 patients with chronic hemodialysis in order to find out the early signs of dialysis encephalopathy. They found 21 patients with abnormal speech, 13 of whom had severe disturbances. Since most of these 13 patients were considered clinically normal in medical investigation, it is obvious that a careful assessment of speech and language functions is important for the early detection of dialysis encephalopathy. This will make it possible to start earlier the treatment with desferrioxamine and the dialysate water purification, which have proved effective in dialysis encephalopathy. In future, the scope of investigations into communicative disorders has to be broadened to other metabolic diseases in order to increase our knowledge about neurogenic dysfluencies.

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